

EXHIBIT D

Product Safety Labs

STUDY TITLE

Azoxystrobin 96% Technical:
Characterization of Active Ingredient in a Sample of Test Substance

AUTHOR

William D. Gravelle, MS

STUDY COMPLETED ON

September 7, 2016

PERFORMING LABORATORY

Product Safety Labs

LABORATORY STUDY NUMBER

43396

SPONSOR

Whiteford, Taylor & Preston LLP
7 St. Paul Street
Baltimore, Maryland 21202

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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

Azoxystrobin 96% Technical

This study meets the requirements of 40 CFR Part 160: U.S. EPA (FIFRA), 1989 with the following exception:

Characterization of the reference substance was not documented according to GLP, however, the purity of the material used was certified by a reputable supplier.

Other than analyses conducted at Product Safety Labs, specific information related to the characterization of the test substance as received and tested is the responsibility of the study Sponsor (see Test Substance section).

Study Director: William D. Gravelle

Date: 9/7/2016

Name of Signer: William D. Gravelle, MS

Name of Company: Product Safety Labs

QUALITY ASSURANCE STATEMENT

The Product Safety Labs' Quality Assurance Unit has reviewed this final study report to assure the report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the study.

QA activities for this study:

QA Activity	Date Conducted	Date Findings Reported To Study Director And Management
Protocol review	Apr 20, 2016 ¹ ; Aug 30, 2016	Apr 20, 2016; Aug 31, 2016
In-process inspection: <i>Standard preparation at Day 14</i>	Aug 22, 2016	Aug 22, 2016
Raw data audit	Aug 30-31, 2016	Aug 31, 2016
Draft report review	Aug 30-31, 2016	Aug 31, 2016

Final report reviewed by:

Michelle Hendrickson

Michelle Hendrickson, BA
Quality Assurance Auditor
Product Safety Labs

Sept. 07, 2016

Date

¹ PSL's "generic" protocol used for this study was reviewed by Quality Assurance on this date.

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AZOXYSTROBIN 96% TECHNICAL: CHARACTERIZATION OF ACTIVE INGREDIENT IN A SAMPLE OF TEST SUBSTANCE

PROTOCOL NO.:	P803
AGENCY:	EPA (FIFRA)
STUDY NUMBER:	43396
SPONSOR:	Whiteford, Taylor & Preston LLP 7 St. Paul Street, Baltimore, MD 21202
TEST SUBSTANCE IDENTIFICATION:	Azoxystrobin 96% Technical Batch # WA20160107
DATE RECEIVED:	May 18, 2016
PSL REFERENCE NO.:	160518-6H
STUDY INITIATION DATE:	August 5, 2016
DATES OF TEST:	August 5, 2016 – August 23, 2016
NOTEBOOK NO.:	16-43396 pgs. 1-71

1. PURPOSE

The objective of this study was to determine the level of 1,4-Diazabicyclo[2.2.2]octane (DABCO) in a sample of Azoxystrobin 96% Technical (see Amendment 1). The results of this study can be used to demonstrate the level of this impurity of a sample of the test substance.

2. MATERIALS

A. Test Substance

The test substance, identified as Azoxystrobin 96% Technical, Batch: WA20160107, was received on May 18, 2016 and was further identified with PSL Reference Number 160518-6H. The test substance was received from Sino-Agre Leading Biosciences Co., Ltd., F9 Building C, Global Finance & News Center, No. A1, Xuanwumenwai Street, Beijing, China 100052 whom, we have been told, acquired it from Yancheng Tai He Chemicals Co., Ltd located in Yancheng, China. The test substance was stored at room temperature prior to initiation of the study.

The following information related to the characterization of the test substance was provided by the Sponsor unless otherwise noted:

Composition: Not provided

Physical description: Off-white powder

pH: 4.9

Stability: Test substance was expected to be stable for the duration of testing.

Expiration Date: January 6, 2018

Any additional test substance is retained for at least 3 months following completion of the final report, unless otherwise specified by the Sponsor. After this time period all remaining test substance will be returned to the Sponsor or properly disposed.

3. PROCEDURE

A. Chemical Analysis

The test substance was analyzed for the level of 1,4-Diazabicyclo[2.2.2]octane (DABCO) by Liquid Chromatography - Mass spectrometry (LC/MS/MS). A detailed description of the analytical test method was documented at the time of initial characterization.

3.A.1 Reference Standard

Name: 1,4-Diazabicyclo[2.2.2]octane (DABCO) – Reagent Plus, ≥ 99%

Batch No.: WXBC2101V

Purity: 99.6%

Expiration Date: June 24, 2017

Supplied by: Sigma-Aldrich

3.A.2 Solution Preparation:

Standard Preparation: Duplicate stock reference standard solutions were prepared by accurately weighing approximately 10 mg of the reference standard into separate 100 mL volumetric flasks, dissolving in and diluting to volume with acetonitrile, and mixing well.

Linearity Working Standard Preparation: Six working standard solutions were prepared by pipetting appropriate amounts of the stock or working reference standard solutions into appropriately sized volumetric flasks, diluting to volume with acetonitrile, and mixing well. Aliquots were transferred to appropriate auto sampler vials for analysis. The target concentration ranged from approximately 5 – 500 ng/mL, roughly equivalent to 0.26 – 26 µg/g of test substance.

Calibration ID	Stock or Working Standard Vol. (mL)	Vol. Flask Vol. (mL)	Stock Std.
Lin 1	5	10	Lin 2
Lin 2	1	10	Lin 4
Lin 3	1	10	Lin 5
Lin 4	0.1	100	DABCO-1
Lin 5	5	10	Lin 6
Lin 6	0.5	100	DABCO-2

Accuracy Sample Preparation: In replicate, approximately 1.0 g of test substance was weighed into separate 50 mL volumetric flasks to which a portion of acetonitrile was added. Appropriate amounts of the stock reference standard was added to give two spike levels with nominal concentrations of 10 and 50 ng/mL. Five replicate samples were prepared for the Low spike and two replicate samples were prepared for the High spike level. The amount of DABCO

recovered in the spikes samples was compared to the expected amount and the percent recovery was determined.

Test Substance Preparation: In replicate (n=5), approximately weigh 1.0 g of test substance was weighed into separate 50 mL volumetric flasks, dissolved in and brought to volume with acetonitrile, and mixed well.

3.A.3 Method Validation:

Linearity: Linearity was evaluated by analyzing duplicate injections of the six linearity preparations at test initiation. Linear regression of the calibration curve gave a correlation coefficient (*r*) of 0.9989. A correlation coefficient value of ≥ 0.995 is considered acceptable.

Limit of Quantitation (LOQ): The LOQ was determined from the peak area response resulting from seven injections of the Lin 2 working standard solution described in Section 3.A.2. The relative standard deviation (RSD) of the area response was compared to the modified Horwitz limit. The RSD was 8.0%. An RSD value less than the modified Horwitz limit indicated the concentration of this standard (10.5 ng/mL, or 0.6 $\mu\text{g/g}$ ¹) is an acceptable LOQ.

Accuracy: The average amount of DABCO recovered in the spiked samples was 121 and 96.7% for the Low and High Spike samples, respectively. The average overall recovery was 108.9%. A recovery of 75-125% is considered acceptable for impurity levels less than 0.1% or 0.0001 $\mu\text{g/g}$.

Precision: Method precision was determined from the relative standard deviation (RSD) of the percent recovery value resulting from five replicate preparations of the Low spike sample, which was spiked at a level equivalent to the method LOQ. The RSD value obtained was 7.3%. An RSD less than 10% is considered acceptable.

3.A.4 Analysis:

An analysis sequence was prepared containing solvent blanks, linearity solutions, and spike/assay preparations. Duplicate injections of each test substance preparation and at least two total injections of each linearity preparation were performed. The peak area response was recorded. The amount of active ingredient found was calculated as shown below.

3.A.5 Calculation

$$\text{DABCO } (\mu\text{g/g}) = \text{Calc. Conc. (ng/mL)} / \text{Sample Conc. (ng/mL)} \times \text{CF}$$

Where: Sample Conc. (ng/mL) = Sample Weight (mg) / Extract Vol. (mL) \times CF2

DABCO Calc. Conc. in Extract (ng/mL) = (Peak Area - Intercept) / Slope

CF1 = Conversion Factor = 10^6 ng/ μg

CF2 = Conversion Factor = 10^6 $\mu\text{g}/\text{mg}$

Modified Horwitz limit = $0.67 \times 2^{(1-0.3 * (\text{LOG10}(\text{conc in test substance } (\mu\text{g/g}) / 1000000)))}$

B. Observations

The physical appearance of the material was observed and recorded.

¹ Equivalent concentration in the test substance.

4. STATISTICAL ANALYSIS

Calculation of a mean, standard deviation, relative standard deviation, correlation coefficient (r), and the modified Horwitz limit were the only statistical methods employed for analyzing the data.

5. STUDY CONDUCT

This study was conducted at Product Safety Labs' (PSL) test facility at 2394 US Highway 130, Dayton, New Jersey 08810. The Study Director for this study was William D. Gravelle, MS. The primary chemist for this study was Michael James, BS. This study was conducted to comply with the Good Laboratory Practice (GLP) regulations as defined in:

- 40 CFR 160: U.S. EPA GLP Standards: Pesticide Programs (FIFRA)

and based on the following testing guidelines:

- No OPPTS guideline exists for the characterization of active in a sample of test substance. The testing described in this protocol is designed to satisfy U.S. EPA GLP Standards 40 CFR Part 160.105(a).

6. QUALITY ASSURANCE

The final report was audited for agreement with the raw data records and for compliance with the protocol, Product Safety Labs Standard Operating Procedures and appropriate Good Laboratory Practice Standards. Dates of inspections and audits performed during the study and the dates of reporting of the inspection and audit findings to the Study Director and Facility Management are presented in the Quality Assurance Statement.

7. AMENDMENT TO THE PROTOCOL

The purpose of the study was clarified to indicate that the level of 1,4-Diazabicyclo[2.2.2]octane (DABCO) in a sample of Azoxystrobin 96% Technical was to be determined, not the level of the active ingredient.

8. DEVIATIONS FROM THE FINAL PROTOCOL

None.

9. FINAL REPORT AND RECORDS TO BE MAINTAINED

Information on equipment maintenance and calibration, storage, usage, and disposition of the test substance, and all other records that would demonstrate adherence to the protocol will be maintained. Facility records which are not specific to the subject study will be maintained by the testing facility and archived according to PSL SOP.

The original, signed final report will be forwarded to the Sponsor. A copy of this signed report, together with the protocol and all raw data generated at Product Safety Labs, is maintained in the Product Safety Labs Archives. Product Safety Labs will maintain these records for a period of at least five years. After this time, the Sponsor will be offered the opportunity to take possession of the records or request continued archiving by Product Safety Labs.

10. RESULTS

HPLC operating conditions are recorded in Table 1. Linearity results are presented in Table 2. Results of test samples analyzed are presented in Table 3. Representative chromatograms are presented in Appendix A.

Azoxystrobin 96% Technical was observed to be an off-white powder.

Test Substance ID	Impurity	(Mean)
Azoxystrobin 96% Technical Batch #: WA20160107	1,4-Diazabicyclo[2.2.2]octane, µg/g	None detected

SIGNATURE

Azoxystrobin 96% Technical

I, the undersigned, declare that the methods, results and data contained in this report faithfully reflect the procedures used and raw data collected during the study.



William D. Gravelle, MS
Study Director
Product Safety Labs



Date

TABLE 1: HPLC OPERATING CONDITIONS

System	Agilent 1100 HPLC w/ AB Sciex 4000
Column	Agilent Zorbax Aq, 4.6 x 250 mm, 5 μ
Elution	Gradient (see table below)
Injection Volume (μL)	50
Run Time (minutes)	20
Flow rate (ml/min)	1.0
Column Temperature (°C)	20
DABCO Retention Time (min):	~ 2.0
MS conditions	
Scan type	MRM*
Ionization/mode	Electrospray/ positive
Q1 mass (Da)	113.17
Q3 mass (Da)	84.1
Ion spray voltage, (V)	5000

*Multiple Reaction Monitoring

Mobile phase gradient configuration:

Time (minutes)	0.1% Formic Acid in DI Water (%)	Acetonitrile (%)
0.0	80	20
3.5	80	20
3.6	5	95
15.0	5	95
15.1	80	20
20.0	80	20

TABLE 2: METHOD VALIDATION RESULTS

Linearity

Standard #	Concentration (ng/mL)	Peak Area	Equivalent concentration in test substance (µg/g)	
Lin 1 ¹	5.23	984	0.4	
		1150	0.4	
Lin 2	10.46	2547	0.6	
		2405	0.6	
Lin 3	26.64	5154	1.0	
		5302	1.0	
Lin 4	104.58	39534	6.1	
		36287	5.7	
Lin 5	266.43	83613	12.7	
		83333	12.7	
Lin 6	532.86	176777	26.6	
		179687	27.1	
Correlation Coefficient (r)			0.9989	
Slope			334.96	
Intercept			-1573.21	

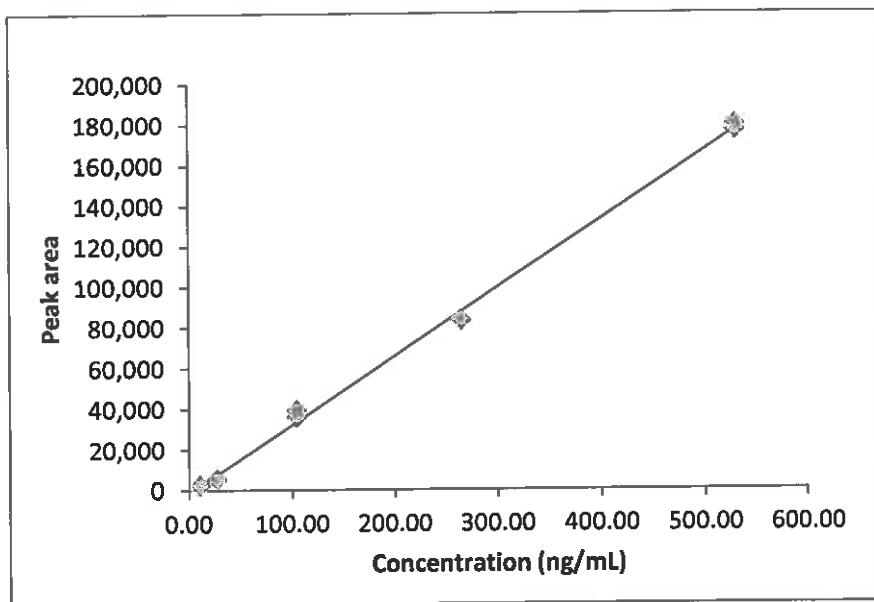
¹ Excluded from calibration curve as the response was weak (less than 10X signal:noise ratio)

TABLE 2 (cont): METHOD VALIDATION RESULTS

Accuracy

Sample ID	Test substance wt (mg)	Test Substance Conc. (ng/mL)	Area	Measured Conc. (ng/mL)	Expected Conc. (ng/mL)	Recovery (%)	Average Recovery / SD /RSD (%)
Spike 1-1-1	1004.6	20092000	2562	12.345	10.657	115.8	121.0 8.8 7.3
Spike 1-1-2	1004.6	20092000	2678	12.692	10.657	119.1	
Spike 1-2-1	1011.4	20228000	3068	13.856	10.657	130.0	
Spike 1-2-2	1011.4	20228000	2946	13.492	10.657	126.6	
Spike 1-3-1	1018.1	20362000	3166	14.149	10.657	132.8	
Spike 1-3-2	1018.1	20362000	3073	13.871	10.657	130.2	
Spike 1-4-1	1009.9	20198000	2791	13.029	10.657	122.3	
Spike 1-4-2	1009.9	20198000	2601	12.462	10.657	116.9	
Spike 1-5-1	1021.1	20422000	2276	11.492	10.657	107.8	
Spike 1-5-2	1021.1	20422000	2313	11.602	10.657	108.9	
Spike 2-1-1	1027.5	20550000	16187	53.022	53.286	99.5	96.7 2.5 2.6
Spike 2-1-2	1027.5	20550000	15134	49.879	53.286	93.6	
Spike 2-2-1	1048.2	20964000	15849	52.013	53.286	97.6	
Spike 2-2-2	1048.2	20964000	15562	51.156	53.286	96.0	
Overall average							108.9

Slope = 334.96

Intercept = -1573.21

TABLE 3: RESULTS OF TEST SAMPLE ANALYSIS**1,4-Diazabicyclo[2.2.2]octane (DABCO) content ($\mu\text{g/g}$)**

Sample ID	Sample Conc. (ng/mL)	Peak Area	DABCO Calc. Conc. in extract (ng/mL)	DABCO in test substance ($\mu\text{g/g}$)	Mean \pm SD
6H-1	20374000	483 ¹	0.00	< LOQ	< LOQ
		0	0.00	< LOQ	
6H-2	20162000	0	0.00	< LOQ	< LOQ
		0	0.00	< LOQ	
6H-3	20008000	0	0.00	< LOQ	< LOQ
		0	0.00	< LOQ	
6H-4	23232000	0	0.00	< LOQ	< LOQ
		0	0.00	< LOQ	
6H-5	20094000	0	0.00	< LOQ	< LOQ
		0	0.00	< LOQ	

Slope = 334.96; y-intercept = -1573.21

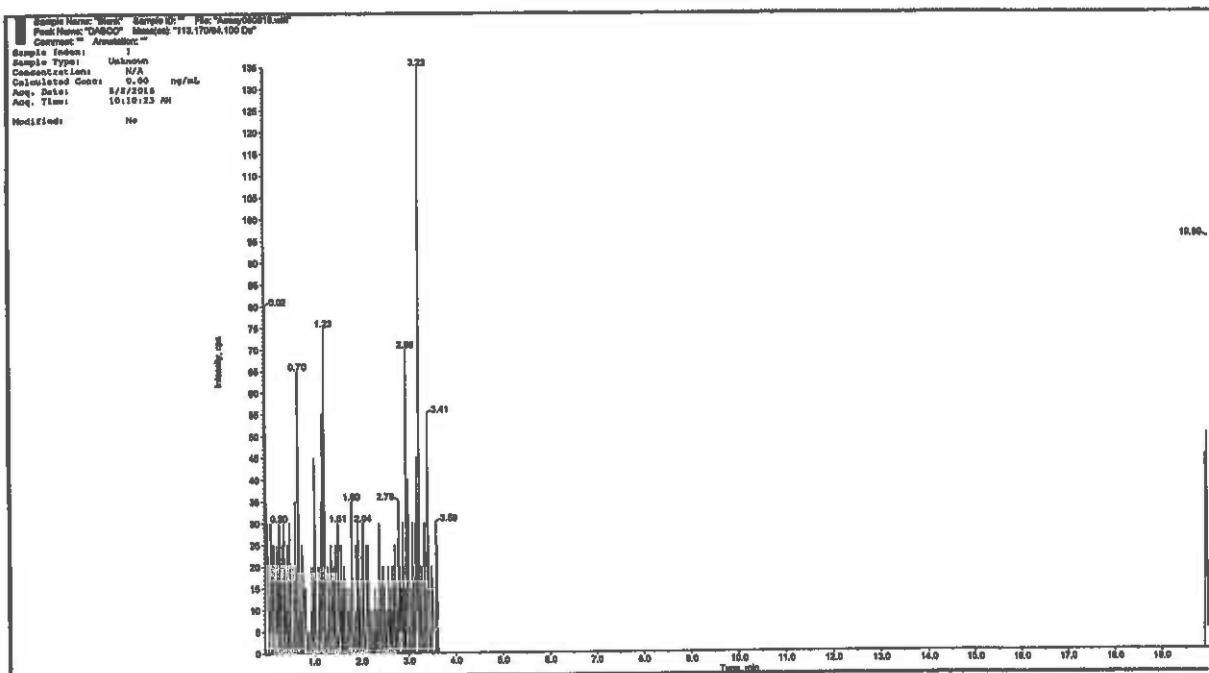
¹ Response is less than Limit of Quantitation or 0.6 $\mu\text{g/g}$. The signal obtained is likely due to carryover from the highest calibration standard of 532 ng/mL. The lack of a DABCO signal in the remaining injections indicates it is not likely due from the sample.

APPENDIX A: REPRESENTATIVE CHROMATOGRAMS

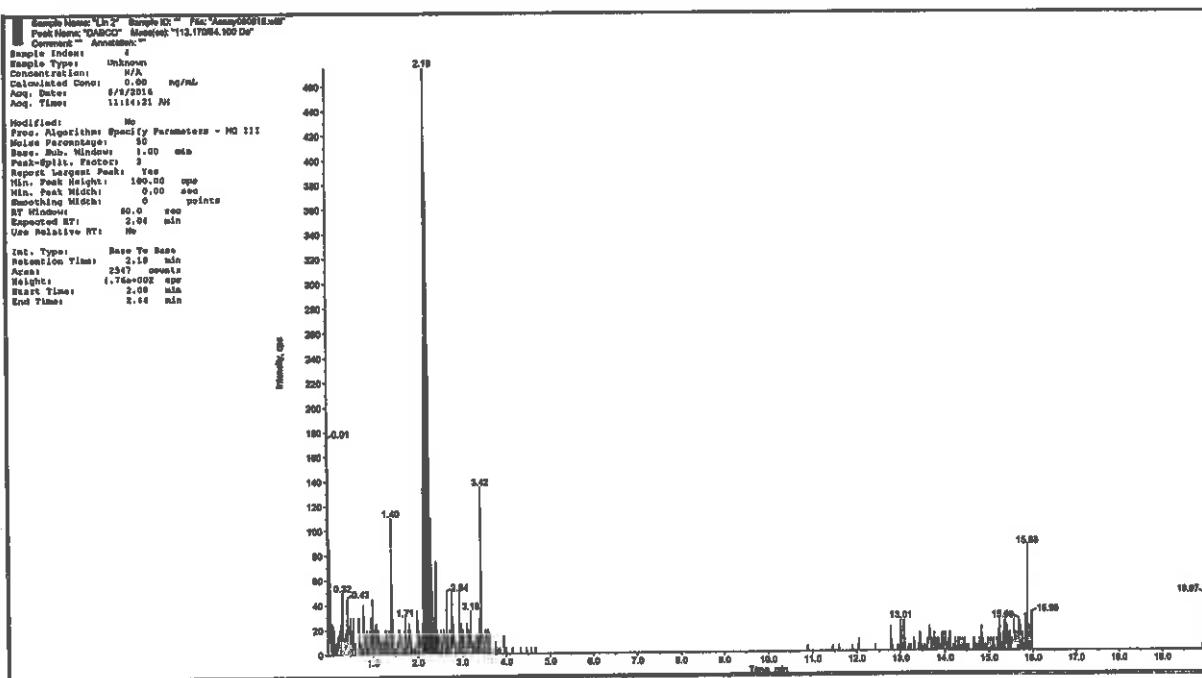
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Sample Number: Sample 1 of 50

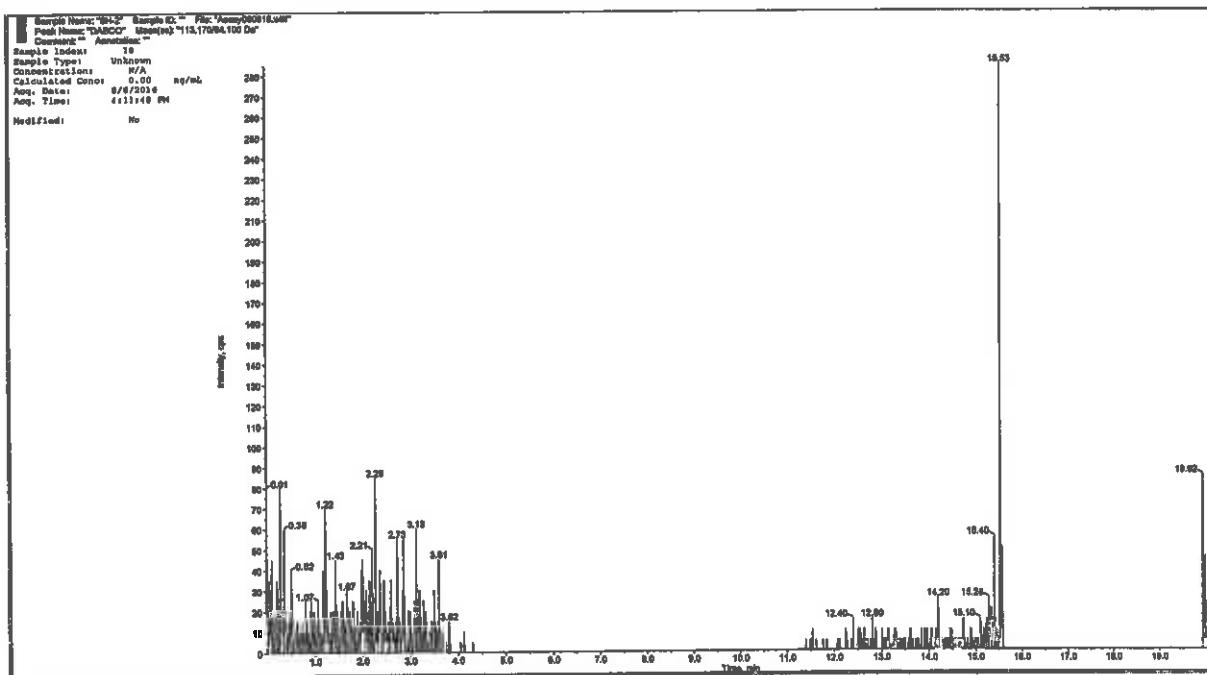


APPENDIX A (cont.): REPRESENTATIVE CHROMATOGRAMS DABCO STANDARD, 10.46 ng/mL



APPENDIX A (cont.): REPRESENTATIVE CHROMATOGRAMS

TEST SUBSTANCE, (20000000 ng/mL)



APPENDIX A (cont.): REPRESENTATIVE CHROMATOGRAMS TEST SUBSTANCE SPIKED AT DABCO CONC OF 10.66 ng/mL)

